

Claims

10/19/98  
6/10/10/99 if this is entered in patent.

What is claimed is:

1. A stabilized lyophilized hepatitis A live vaccine formulation comprising a prophylactically effective titers of live attenuated hepatitis A virus and a stabilizer, wherein said stabilizer ~~being~~ is present in the vaccine formulation at a concentration sufficient to ~~stabilizer~~ stabilize the hepatitis A virus against heat inactivation.

2. A stabilized lyophilized hepatitis A vaccine formulation according to claim 1, wherein said live attenuated hepatitis A virus is prepared ~~by disclosed method based on~~ from the wide wild-type HAV, stain strain L-A-I.

3. A stabilized lyophilized hepatitis A live vaccine formulation according to claim 1, wherein said stabilizer for lyophilized live hepatitis A virus comprises essentially composed of human serum albumin or gelatin or both of them, trehalose, at least one ~~or two~~ amino acid selected from the group consisting of glutamic acid, aspartic acid, arginine, lysine or alkali metal salts thereof, ascorbic acid, urea, mannitol or sorbitol or both of them, and inositol.

4. A stabilized lyophilized hepatitis A live vaccine formulation according to claim 1, wherein said stabilizer for lyophilized live virus ~~vaccine~~ may optionally ~~contains~~ contain human serum albumin.

5. A stabilized lyophilized hepatitis A live vaccine formulation according to either one of claim 3 or 4, wherein said stabilizer for the lyophilized live virus comprises essentially composed of from 0 to 20 grams per liter of human serum albumin, from 5 to 10 grams per liter of gelatin, from 50 to 100 grams per liter of trehalose, from 7.5 to 15 grams per liter of sodium glutamate, from 0.5 to 5.5 grams per liter of ascorbic acid, from 5 to 28 grams per liter of urea, from 2 to 10 grams per liter of mannitol or sorbitol, from 4 to 10 grams per liter of inositol.

)

6. A method of preparing stabilized lyophilized liver hepatitis A vaccine formulation according to any one of the claims 1 to 5, comprising:

- (a) providing a stock suspension of attenuated liver Hepatitis A virus,
- (b) adding a stabilizer solution to stock suspension of attenuated live hepatitis A virus obtained from step (a) at the ratio 1:1 (v/v) to obtain a live vaccine formulation comprising prophylactically effective titers of live attenuated hepatitis A virus and a stabilizer for attenuated live virus, wherein said stabilizer comprises gelatine, thehalose, one or two amino acid selected from the group consisting of glutamic acid, ~~aspartic~~ aspartic acid, arginine, lysine or alkali metal salts thereof, ~~ascorbic~~ ascorbic acid, urea, mannitol or sorbitol or a mixture of them, and inositol.
- (c) lyophilizing said vaccine formulation obtained from the step (b).

7. A stabilizer for lyophilized live virus, wherein said stabilizer comprises essentially ~~composed of~~ gelatin, trehalose, at least ~~one or two~~ amino acid selected from the group consisting of glutamic acid, aspartic acid, arginine, lysine or alkali metal salts thereof, ascorbic acid, urea, mannitol or sorbitol or a mixture of them, and inositol.

8. A stabilizer according to claim 7, wherein said stabilizer comprises essentially ~~composed of~~ from 0 to 20 grams per titer of human serum albumin, from 5 to 10 grams per liter of gelatin, from 50 to 100 grams per liter of trehalose, from 7.5 to 15 grams per liter of sodium glutamate, from 0.5 to 5.5 grams per liter of ascorbic acid, from 5 to 28 grams per liter of urea, from 2 to 10 grams per liter of mannitol or ~~sorbital~~ sorbitol, and from 4 to 10 grams per liter of inositol.

9. A stabilizer according to claim 7, wherein said stabilizer for lyophilized live virus vaccine ~~may optionally contains~~ further comprises human serum albumin.

10. A stabilizer according to claim 7, wherein said ~~stabilizer not only suitable for stabilizing lyophilized hepatitis A live virus, but also used for protecting viruses~~ virus is selected from the group consisting of genus Enterovirus, ~~the genres~~ Papamylavirus Pavamyxovirus, the genus Arbovirus, and ~~the genus~~ Herpesvirus Herpesvirus against heat inactivation during the period of lyophilization and the period of storage and transportation post-lyophilization and the period of storage and transportaion post-lyophilization to ensure thermo-stability of the lyophilized live vaccine thereby to improve vaculation efficacy for susceptible population.